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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,823	DEBINSKI ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 18-43* is/are pending in the application.

4a) Of the above claim(s) *2-8 and 19-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-14 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-14, and 18-43 are pending.

2. Claims 2-8 and 19-43 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. Claims 1, 9-14 and 18, drawn to a method for detecting a cancer in a brain tissue for a VEGF-D protein marker using a probe wherein the probe is a VEGF-D antibody, are being acted upon in this Office Action.

4. The following new grounds of rejections are necessitated by the amendment filed 1/18/06.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

6. Claims 1 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The "*analyzing* the brain tissue..." in claim 1 (C) does not referred back to the preamble of a method for *detecting* in claim 1.

The "VEGF-D marker" in claim 9 has no antecedent basis in base claim 1. Base claim 1 recites VEGF-D protein, not marker.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 9-11, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,235,713 B1 (of record, filed Aug 1997; PTO 892) in view of US Pat No. 5,874,290 (of record, Feb 1999; PTO 892), Hamel et al (Acta Neurochirugica 142: 113-138, 2000; PTO 892), Wesseling et al (J Neurosurg 81(6): 902-9, Dec 1994; PTO 892) and Amalfitano et al (Cancer Genet Cytogenet 116: 6-9, 2000; PTO 892).

The '713 patent teaches a method of detecting VEGF-D in a biological sample comprising the steps of contacting the sample with a probe such as labeled monoclonal antibody that binds specifically to the native full length human VEGF-D (see col. 6, lines 66-67 bridging col. 7, lines 1-7, col. 5, lines 51-67, in particular). The reference VEGF-D is a native VEGF-D protein (see col. 19, lines 34-42, VEGFD full FLAG, in particular) and could be proteolytic cleaved to form the VEGF-D homology domain (see col. 19, line 25, VEGFDΔNΔC, in particular). The '713 patent teaches VEGF-D is located on the X chromosome in band p22.1 (see col. 24, lines 1-8, in particular) and is useful as a clinical diagnostic marker in cancer biopsy specimens and is an indicator of future metastatic risk (see col. 6, lines 16-18, in particular). The '713 patent further teaches a method of detecting the aberrations in VEGF-D located on the X chromosome (see col. 7, lines 40-43, in particular).

The invention differs from the teachings of the reference only in that the method for detecting a glioblastoma multiforme in a brain tissue sample instead of any biological sample.

The invention in claim 13 differs from the teachings of the reference only in that the method wherein the brain tissue sample comprises a cell exhibiting abnormal ploidy for chromosome X.

The '290 patent teaches various VEGFs that have been shown to overexpressed in different types of brain tumors (see col. 3, lines 5-14, and references therein, in particular). The '290 patent further teaches the use of human cell lines derived from glioblastoma multiforme

tumor tissue and a method of diagnosis of brain tumor using VEGF as markers (see col. 25, line 55, col. 43, lines 35-62, in particular).

Hamel et al teach gliomas are among the most vascularized tumors in man (see page 121, col. 1, first paragraph, in particular). Hamel et al further teach VEGF is expressed abundantly in high grade gliomas (see page 121, col. 1, first full paragraph, in particular).

Wesseling et al teach human glioblastoma multiforme has significant increase in mean number, area and perimeter of blood vessels per microscopic filed compared with those in histologically normal cerebral cortex and white matter (see abstract, in particular). Wesseling teach the use of brain tissue sample from glioblastoma multiforme and normal tissue for comparison (see materials and methods, abstract, in particular).

Amalfitano et al teach numerous chromosomal abnormalities such as X chromosome, chromosome 7 and 10 have been detected in human glioblastoma multiforme (see page 6, col. 1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to detect the overexpression of VEGF-D protein as taught by the '290 patent in brain tissue from patient with glioblastoma multiforme as taught by Wesseling et al using the labeled anti-VEGF-D antibody as taught by the '713 patent since VEGF is expressed abundantly in high grade gliomas as taught by Hamel and numerous chromosomal abnormalities have been detected in human glioblastoma multiforme as taught by Amalfitano et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '290 patent teaches various VEGFs have been shown to overexpressed in different types of brain tumors (see co. 3, lines 5-14, and references therein, in particular). Hamel et al teach gliomas are among the most vascularized tumors in man (see page 121, col. 1, first paragraph, in particular). Hamel et al further teach VEGF is expressed abundantly in high grade gliomas (see page 121, col. 1, first full paragraph, in particular). VEGF-D is useful as a clinical diagnostic marker in cancer biopsy specimens and is an indicator of future metastatic risk as taught by the '713 patent (see col. 6, lines 16-18, in particular). One having ordinary skill in the art would have been motivated with the expectation that the VEGF-D expression would be overexpressed in highly vascularized tumor such as human glioblastoma multiforme as taught by Wesseling et al. Claim 13 is included in this rejection because abnormal ploidy for chromosome X in human glioblastoma

multiforme is to be expected since Amalfitano et al teach numerous chromosomal abnormalities have been detected in human glioblastoma and the '713 patent teaches VEGF-D is located on the X chromosome in band p22.1 (see col. 24, lines 1-8, in particular).

Applicants' arguments filed 1/18/06 have been fully considered but are not found persuasive.

Applicants' position is that the '713 patent does not teach or suggest that VEGF-D is detected in brain tissue samples. Hamel et al do not teach or disclose the detection of VEGF-D in glioblastomas in brain tissue samples. Considering the different VEGFs have different chromosomal localizations, one of ordinary skill in the an would not expect that just one type of VEGFs is found in cancer, the detection of another factor is expected or obvious. The '290 patent does not teach or disclose that VEGF-D is over-expressed in tumors. VEGF was detected in some brain tumors but the '290 patent does not teach or disclose detection and overexpression of VEGF-D as a diagnostic marker of brain tumors isolated from human brain tissue sample. The '290 patent utilized established cell lines for detection of the D2-2 gene (see for example 43, lines 49-62). The fetal brain tissue is not a tumor and consequently cannot be used as a tool to diagnose brain tumors.

In response, this rejection would be rejected under 35 U.S.C. 102(b) had the '713 patent or the '290 patent teaches VEGF-D is detected in glioblastoma multiforme of brain tissue samples. However, the '713 teaches VEGF-D is a marker for cancer in tissue sample and a method of detecting VEGF-D in tissue sample using antibody that binds to human VEGF-D. The '713 patent further teaches VEGF-D is located on X-chromosome (see col. 7, lines 40-43, in particular).

Hamel et al teach gliomas are among the most vascularized tumors in man (see page 121, col. 1, first paragraph, in particular). Hamel et al further teach VEGF is expressed abundantly in high grade gliomas would have led to one of ordinary skill in the art at the time the invention was made to detect VEGF-D in gliomas such as human glioblastoma multiforme using the labeled antibody that binds specifically to VEGF-D as taught by the '713 patent.

In response to the argument that the '290 patent utilized established cell lines instead of brain tissue sample, Wesseling et al teach the use of brain tissue sample from glioblastoma multiforme and normal tissue for comparison (see materials and methods, abstract, in particular). The '290 patent teaches various VEGFs that have been shown to overexpressed in different types of brain tumors (see col. 3, lines 5-14, and references therein, in particular).

10. Claims 12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 6,235,713 B1 (of record, filed Aug 1997; PTO 892) in view of US Pat No. 5,874,290 (of record, Feb 1999; PTO 892), Hamel et al (Acta Neurochirugica 142: 113-138, 2000; PTO 892), Wesseling et al (J Neurosurg 81(6): 902-9, Dec 1994; PTO 892) and Amalfitano et al (Cancer Genet Cytogenet 116: 6-9, 2000; PTO 892) as applied to claims 1, 9-11, and 13-14 and further in view of Achen et al (of record, Eur. J. Biochem. 267: 2505-2515, May 2000; PTO 1449).

The combined teachings of the '713 patent, the '290 patent, Hamel et al, Wesseling et al and Amalfitano et al have been discussed supra.

The invention in claims 12 and 18 differs from the combined teachings of the references only in that the method for detecting glioblastoma multiforme wherein the monoclonal antibody binds to the homology domain of human VEGF-D instead of the native full-length human VEGF-D.

Achen et al teach various monoclonal antibodies such as VD1, VD2, VD3 and VD4 that bind specifically to the homology domain of human VEGF-D (see page 2507, col. 2, Results, production of anti-VEGF-D mAbs, page 2508, col. 2, last paragraph, in particular). Achen et al teach antibody such as VD2 also binds to the native VEGF-D protein (see page 2508, col. 2, in particular) and the VEGF-D homology domain (see page 2511, col. 1, in particular). Achen et al teach the reference antibody could block the mitogenic response of vascular endothelial cells to VEGF-D (see page 2512, col. 1, in particular) and strongly inhibits the binding of VEGFDΔNΔC or the VEGF-D homology domain (VHD) to both VEGFR2 and VEGFR3 (see page 2511, col. 1, last par, in particular). Achen et al teach that these antibodies are useful for analyzing angiogenesis induced by VEGF-D and its contribution to metastatic spread (see page 2513, col. 1, last paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the monoclonal antibody that binds to native full-length human VEGF-D as taught by the '713 patent for the VD2 monoclonal antibody that binds specifically to the native and/or VEGF-D homology domain (VHD) of human VEGF-D as taught by Achen et al for a method of detecting glioblastoma multiforme in brain tissue as taught by the '713 patent, the '290 patent, Hamel et al, Wesseling et al and Amalfitano et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Achen et al teach VD2 monoclonal antibody is specific to VHD of human VEGF-D and is useful for analyzing angiogenesis induced by VEGF-D and its contribution to cancer (see page 2513, col. 1, last paragraph, in particular). The '290 patent teaches various VEGF have been shown to overexpressed in different types of brain tumors (see co. 3, lines 5-14, and references therein, in particular). The '713 patent teaches VEGF-D is useful as a clinical diagnostic marker in cancer biopsy specimens (see col. 6, lines 16-18, in particular).

Applicants' arguments filed 1/18/06 have been fully considered but are not found persuasive.

Applicants' position is that arguments regarding the combined teachings of '713 and '290 and Hamel et al have been discussed supra. Achen el al standing alone or in combination teaches the detection of a native protein VEGF-D homology domain in brain cancer. None of the references teach the detection of VEGF-D in the brain nor was the form of VEGF-D in the brain known prior to applicant's invention.

In response, Achen el al teach antibody that binds to the homology domain of human VEGF-D. The combined teachings of the '713 patent, the '290 patent, Hamel et al, Wesseling et al and Amalfitano et al as discussed supra would have led to one of ordinary skill in the art to detect VEGF-D in glioblastoma multiforme using antibody that binds to the homology domain of human VEGF-D as taught by Achen et al since VEGF-D could be proteolytic cleaved to form the VEGF-D homology domain as taught by the '713 patent (see col. 19, line 25, VEGFDΔNΔC, in particular) and Achen et al.

Hamel et al teach gliomas are among the most vascularized tumors in man (see page 121, col. 1, first paragraph, in particular). Hamel et al further teach VEGF is expressed abundantly in high grade gliomas would have led to one of ordinary skill in the art at the time the invention was made to detect VEGF-D in gliomas such as human glioblastoma multiforme using the labeled antibody that binds specifically to VEGF-D as taught by the '713 patent.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

14. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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